include these effects and this appears not to influence results in general. More empirical work is needed, using generic instruments, larger and more relevant samples, and perhaps using the interview method of administration.

PMC16

EXPENSIVE DRUGS FOR RARE DISORDERS AND THE LOGIC OF COST-EFFECTIVENESS

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OBJECTIVES: Expensive drugs for rare disorders (EDRDs; "orphan drugs") do not usually meet widely applied cost-effectiveness benchmarks ("lambdas"). Adopting the standard decision rules of the logic cost-effectiveness cannot be reconciled with granting reimbursement status for many EDRDs and would inevitably deprive patients with very rare disorders from any chance to get access to effective treatment, given the high fixed / low variable cost structure of the pharmaceutical industry. On the other hand, public policies have been established to provide incentives to support development of orphan drugs. This (and some further observations) suggests a serious mismatch between the logic of cost-effectiveness and societal preferences. Decision-makers have responded; for instance, the National Institute for Health and Clinical Excellence (NICE) attempts to define a special subcategory of "ultra-orphans"—while maintaining that budgetary impact analysis is not part of its appraisal decisions (but limited to implementation support). This policy, however, does not appear to adequately address the underlying problem. **METHODS:** First, "ultra-orphans" are not a distinct, well-defined category—they rather represent one extreme of a continuous spectrum, and "orphan drugs" and some cancer treatments pose the same fundamental problem. Second, size of a patient population eligible for treatment is directly linked to budgetary impact (and hence the opportunity for manufacturers to recoup fixed costs), whereas the logic of cost-effectiveness is impaired by not taking into account the size of the numerator and the denominator of the incremental cost-effectiveness ratio (ICER), which has been described as "the silence of the lambda." Policy makers might address these issues by explicitly taking budgetary impact into account when deciding on maximum reimbursement prices or by price-volume agreements. **RESULTS:** Both approaches, albeit perhaps pragmatic, cannot satisfy from a theoretical economic perspective. **CONCLUSIONS:** Rigorous normative analysis and empirical research are required to further explore the mapping of individual health-related utilities into societal preferences (willingness-to-pay).

CONCEPTUAL PAPERS & RESEARCH ON METHODS—Databases & Management Methods

PMC17

VALIDITY OF ELECTRONIC PRECRIPTION CLAIMS RECORDS: A COMPARISON OF ELECTRONIC PBM CLAIMS RECORDS WITH PHARMACY PROVIDER DERIVED RECORDS

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OBJECTIVES: To determine if and to what extent records obtained from PBM pharmacy claims differ from source documents obtained directly from pharmacy providers. Also this study sought to explore possible associations between patient, pharmacy benefit, and pharmacy provider characteristics and the likelihood a patient would have missing prescription claims. **METHODS:** This study used a cross sectional survey of 1,484 patients residing in a single state with a common pharmacy benefit. Patient profiles describing all prescriptions filled in a pharmacy between January 1, 2002 through June 30, 2002 of these patients were requested directly from their pharmacy providers. Logistic regression was used to explore the factors associated with a person receiving a prescription that did not appear on the PBM claims. **RESULTS:** Of the 1484 eligible recipients sampled, profiles were obtained for 323 (22%) persons and there were analyzable profiles for 315 (21%) persons. Of those 2,977 prescriptions filled for the 315 persons, 207 (7.0%) were missing from the claims files indicating that 93% were captured. Prescription drugs such as iron products, digoxins, diuretics, sulfonylureas, and antigout were more likely to be missing from the PBM claims. Only prescription volume consistently influenced the likelihood a patient would have a missing prescription from the PBM claims (OR = 1.08; 95% CI: 1.05–1.12). **CONCLUSIONS:** Claims obtained from pharmacy benefit companies capture approximately 93% of prescription records when verified with records obtained from pharmacy providers. The rate of missing records from PBM claims does not appear to be meaningfully influenced by most finance based pharmacy benefit design features, however, certain drugs available over the counter and less expensive drugs may have less complete claims records compared to other classes of drugs. Higher prescription utilizers are more likely to have prescription records filled that are not captured by PBMs.

CONCEPTUAL PAPERS & RESEARCH ON METHODS—Modeling Methods

PMC18

CONCEPTUALISING DISEASE: BUILDING UNIFYING MODELS TO SUPPORT THE DEVELOPMENT OF PROS AND COST-EFFECTIVENESS ANALYSES. A CASE STUDY IN ALZHEIMER'S DISEASE (AD)

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OBJECTIVE: The core of a cost effectiveness model should be guided by the underlying disease process, natural history and how particular interventions impact on disease. The development of conceptual models within PRO research is based on the same rationale. The objective of this study was to explore the overlap between cost effectiveness modelling and conceptual models for PROs, using AD as an example. **METHODS:** A conceptual model of AD was reviewed alongside a cost effectiveness model by a team of PRO researchers and health economists. Areas of commonality and divergence were documented and discussed. **RESULTS:** Points of overlap were identified which included the impact of AD on day to day functioning of the patient and associated caregiver burden. This will influence the ability of the caregiver to work and impact on other resource utilisation. This may, also have an impact on the time to institutionalisation, which is a major financial burden in AD. One major area of divergence is the emphasis in economic models on the use of generic quality of life data; whereas conceptual models are commonly developed to measure disease specific PRO burden. **CONCLUSIONS:** The commonalities between PRO conceptual models and health economic models indicates the potential for developing PRO and HE models simultaneously. This is likely to increase the validity of each of the models as well as having a positive impact on related research e.g. through the development of health state utilities. As a next step we are prospectively developing a conceptual model of disease which is specifically

designed to support both the collection of PRO data and the development of an economic model.

PMC19

COST-EFFECTIVENESS ANALYSES OF BEHAVIORAL INTERVENTIONS: TOWARDS A MORE REALISTIC COST-EFFECTIVENESS RATIO BY INCLUDING INTERMEDIATE OUTCOME MEASURES

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OBJECTIVES: Behavioral health interventions traditionally use a simple dichotomous outcome criterion: 'success' or 'failure'. In reality, though, behavior change is a complex process in which several steps towards success are taken. There has been little consideration, however, about whether future behavior change should be incorporated in cost-effectiveness analyses (CEAs). The aim of the present review is to identify and evaluate the usage of cognitive, intermediate outcomes in CEAs of behavioral interventions. **METHODS:** Electronic data sources (PsycInfo, WebofScience, Medline, ScienceDirect and Scopus) were searched for CEAs published before February 2008. **RESULTS:** Most CEAs and CUAs reporting cognitive, intermediate outcomes of behavior change fail to incorporate partial behavior changes. Only nine studies were eligible for inclusion in this review. Smith et al 2007 [1] conducted the only study in which partial behavior change was incorporated in the final outcome by modeling cognitive, intermediate outcomes: the stages of change, derived from the Transtheoretical model (TTM). The TTM is a stage-oriented model that describes the process by which a change in behavior takes place. It describes the readiness to change and the processes employed by individuals to achieve behavioral change. With inclusion of future behavior change, Smith et al showed that the incremental cost-effectiveness ratio declined compared to the standard analysis. **CONCLUSIONS:** The results suggest that CEAs of behavioral interventions can be further optimized by the measurement of intermediate outcomes and use these to determine partial behavior change at the end of an intervention period as well. In other words, when partial behavior change and relapse rates are incorporated in CEAs of behavioral treatments, a more realistic and transparent final outcome can be calculated.

[1] Smith, MY, Cromwell, J, DePue, J, et al. Determining the cost-effectiveness of a computer-based smoking cessation intervention in primary care. Managed Care 2007;16:48–55.

PMC20

QUANTITATIVE APPROACH TO DETERMINE THE EFFECT OF SEGMENTATION ON REVENUE GENERATION, POSITIONING AND PRICING OF PHARMACEUTICALS

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OBJECTIVES: To develop a quantitative model that can determine the effect of segmentation and positioning on revenue generation based on different variables, health economic considerations and pricing scenarios, creating a tool which is easy to use for the first evaluation of options. **METHODS:** Literature review and interviews with industry experts were conducted followed by the development of qualitative framework, logic and the subsequently a quantitative model. The model was tested and validated using real life examples. **RESULTS:** A qualitative model was developed which presents an iterative strategy to align stakeholders' interest with different scenarios of segmentation. From a given asset base of active ingredients, the pharmaceutical company defines therapeutic areas for a component and determines segments within them, evaluating both attractiveness and specific propositions for patients, payers and prescribers in comprehensive scenarios. For the payer's perspective in particular, health economic benefits of the proposed segmentation approach must be contemplated. Following this analysis, objectives and strategies for the chosen segments are developed and a holistic value proposition can be delivered to the market. Ideally, the process should be initiated early during development in order to design clinical trials according to the segmentation strategy. The process should also be monitored throughout the marketing and sales process in order to make improvements, and to react to changes in health care policies or the competitive landscape. Following the qualitative analysis, a quantitative model was developed in Excel that captures the effect of multiple variables such as age, gender, disease severity, co-morbidities, insurance type and multiple price points on revenue generation, positioning and pricing of pharmaceuticals. The model was tested and validated using the example of bipolar disorder (BPD) in women with childbearing potential. A new product with lower teratogenic risks was evaluated along different segmentation scenarios in order to determine improved overall cost-effectiveness when compared to conventional treatments. **CONCLUSIONS:** Segmentation is an important tool that could lead to better revenue generation from the company's perspective and is accepted positively by payers due to optimized budget impact with better health outcomes.

PMC21

ASSESSING THE RELATIONSHIP BETWEEN COMPUTATIONAL SPEED AND PRECISION: A CASE STUDY USING A DISCRETE EVENT SIMULATION MODEL IN DIABETES CARE

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BACKGROUND: In model-based health economic evaluations, to achieve a given level of precision surrounding modelled outputs there is a trade-off between treatment effect estimates and the computational time associated with the programming format used to 'code' the model. **OBJECTIVES:** To explore the relationship between modelled effect size, statistical precision and the computational time associated with two commonly used programming frameworks. **METHODS:** A published and validated cost-utility discrete event simulation (DES) diabetes model (Cardiff model) was programmed in MS Excel with Visual Basic (VB), and more recently reprogrammed in C as with other models in this area, to illustrate the efficiency gains in terms of computational speed achieved under different programming frameworks. A treatment effect of 0.4% HbA1c improvement was applied to a mean cohort profile of 10,000 patients; precision in the predicted number of clinical events was used to assess relative efficiency of VB and C. **RESULTS:** In the C programmed model in order to show a significant difference at the 95% level in the predicted number of events in the control and treatment arms required 50 iterations of the model using mean values. This equated to a model run time of 1 minute. The equivalent number of iterations in VB took 133 minutes to demonstrate a significant difference in the predicted number of events. Typically, one-way sensitivity analysis using this model to explore 40 scenarios would equate to a run time of 40 minutes in C and 5,320 minutes (88.7 hours) in VB. **CONCLUSIONS:** Programming format can impact the computational time associated with running the model with subsequent practical implications for the usability of the model. We conclude that with reasonably complex models,